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10/671,546

09/29/2003

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EXAMINER

WHALEY, PABLO S

ART UNIT

PAPER NUMBER

1631

MAIL DATE

DELIVERY MODE

08/04/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|------------------------------------|--|
| Office Action Summary | Application No. 10/671,546 | Applicant(s) SOME ET AL. | |
| | Examiner PABLO WHALEY | Art Unit 1631 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 April 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,5 and 6 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,5 and 6 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 September 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims Under Examination

Claims 1, 2, 5, and 6 are pending. Claims 3, 4, 7, and 8 have been cancelled.

Priority

This application has been granted the benefit of priority to foreign Japanese document 285102/2002, filed 9/30/2002.

Drawings

Applicant's arguments that the published application [0027] provides sufficient description of the drawings has been considered but is not persuasive. It is noted that applicant's arguments should refer to the instant specification and not published applications, as published applications are not in the application files. The drawings again are objected to under 37 CFR 1.83(a). The MPEP § 608.02(d) states that drawings must show every feature of the invention specified in the claims. Therefore, the data concerning expression quantities must be shown or the feature(s) canceled from the claim(s). In particular, the drawings must show the type of units identifying data concerning expression quantities on the "x axis" and "y axis." No new matter should be entered. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining

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figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Objections

Claims 1 and 5 are objected to because of the following informalities: Claims 1 and 5 recites incorrect sequences of steps. In particular, claim 1 recites steps "i), ii), iii), iv), and iv)", wherein step iv) is repeated. Claims 5 recites steps "i), ii), iii), iii), and iv)", wherein step iii) is repeated. Appropriate correction is required.

Withdrawn Rejections

The rejection of claims 1, 2, 5, and 6 under 35 U.S.C. 112, second paragraph, in the Office action mailed 10/29/2007 is withdrawn in view of applicant's arguments and amendments to claim 1, filed 04/29/2008.

The rejection of claims 1, 3, 5, and 6 under 35 U.S.C. 112, first paragraph, for lack of written description in the Office action mailed 10/29/2007 is withdrawn in view of applicant's arguments filed 04/29/2008.

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The rejection of claims 1, 2, 5, and 6 under 35 U.S.C. 103(a) as being unpatentable over Li et al. in view of in view of Stark et al. and GRAPHING WITH LOGARITHMIC PAPER (GLP) is withdrawn in view of applicant's amendments to claims 1 and 5, filed 04/29/2008.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 5, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quackenbush (Nature Reviews Genetics, June 2001, Vol. 2, p. 418-427), in view of GRAPHING WITH LOGARITHMIC PAPER (Department of Physics, University of Guelph, <http://www.physics.uoguelph.ca/tutorials/GLP>, Published Oct. 1997, p. 1-5).

This new grounds of rejection is necessitated by applicant's amendment of claims 1 and 5, filed 04/29/2008.

Quackenbush teaches methods for normalizing and adjusting gene expression data using normalization factors [Abstract, Box 1, and p.419-420]. In particular, Quackenbush teaches steps for collecting expression data from two different samples [p.419, Col. 2, ¶5]. Quackenbush teaches indicating data from two samples with points plotted on a logarithmic coordinate system [Fig. 1]. Quackenbush teaches obtaining an approximate representation of plotted gene expression points using logarithmic-linear lines [Fig. 1], wherein slope coefficients equal to 1 are calculated and at least one line is shifted about the origin. Quackenbush also teaches calculating expression ratios by dividing a particular gene by its normalized value [p.420, Col. 1], which shows performing division processing. Quackenbush teaches calculating log ratio values (i.e. slope) of 1 [p.420, Col. 2], which shows calculating a coefficient. Quackenbush suggests this method is advantageous for the visual determination of artifacts in gene expression data sets and to illustrate the transformation of the data after normalization [Fig. 1, Data Normalization, and p.420. Col. 1].

Quackenbush does not teach obtaining an approximate representation of plotted points with a straight line " $\log y = \log x + a$ ", with a slope 1, as in claims 1 and 5 (step ii).

Quackenbush does not teach calculating the coefficient 10^a , as in claims 1 and 5 (step iii).

Quackenbush does not teach data concerning expression quantities for a second values that are normalized as y' , where $y' = y/10^a$, as in claims 1 and 5.

GRAPHING WITH LOGARITHMIC PAPER (GLP) teaches methods for graphing data from two separate sources on a logarithmic scale (log-log graphs) [p.4, panel 10]. GLP also teaches equations of the form " $\log y = \log a + b \log x$ " [p.4, panel 9], and methods for re-calculating the coefficients to account for changes in the slope as well as x- and y-intercepts when the data is shifted from the origin [p.4 and 5]. GLP does not specifically teach the equation " $\log y = \log x + a$ ", as in claims 1 and 5 (step ii).

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However, it would be obvious to one of ordinary skill in the art to envisage the equations recited in claims 1 and 5 since GLP teaches a general logarithmic-linear equation for representing shifted and non-shifted data. Furthermore, GLP does not specifically teach representing values according to the equation $y' = y/10^a$. However, it would have been obvious to one of ordinary skill in the art to represent gene expression data according the equation in claims 1 and 5 (step iv), since GLP teaches “base 10” or “base e” logarithms [p.4] and basic algebraic manipulations to solve for slope intercept coefficients using division processes [p.5]

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the normalization process of Quackenbush using the specific logarithmic equations for dealing with shifts in the logarithmic data sets, taught by GLP, since Quackenbush teaches methods for normalizing using linear-logarithmic equations and re-scaling data using division techniques [Fig. 1, and p.420, Box 1]. One of ordinary skill in the art would have been motivated to make this modification in order to compare data sets that cover a wide range of values, as suggested by GLP [p.3] or to make improved visual determinations of artifacts in gene expression data sets, as suggested by Quackenbush [Fig. 1, Data Normalization, and p.420. Col. 1].

Response to Arguments

Rejection under 35 U.S.C. 103(a) over Quackenbush and GLP

Applicant's arguments, filed 04/29/2008, that one of ordinary skill in the art would not have been able to predict claimed method of normalizing data by obtaining the coefficient 10^a have been fully considered but are not persuasive. In response, it is well settled that unexpected results must be

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established by factual evidence. Applicants have not presented any experimental data showing how obtaining the coefficient 10^a and using this result in the normalization process results in an unexpected advantage. Due to the absence of tests comparing applicant's normalization process based division by the coefficient 10^a with those of the closest prior art, applicant's assertion of unexpected results constitute mere argument. See also *In re Linder*, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972; Ex parte George, 21 USPQ2d 1058 (Bd. Pat. Appl. & Inter. 1991).

Applicant's arguments, filed 04/29/2008, that one of ordinary skill in the art would not have been motivated to normalize data according to the claimed method because of the infinite number of ways of normalizing data have been fully considered but are not persuasive. In response, Quackenbush teaches well established methods for normalizing data using logarithms and re-scaling factors [p. 420, Box 1, Fig. 1]. Furthermore, GLP teaches general logarithmic equations for representing data in "base 10" or "base e" logarithms. As the claims are limited to normalization using logarithmic equations, GLP teaches there are only a finite number of possibilities for manipulating such equations.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached at 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Pablo S. Whaley/

Patent Examiner

Art Unit 1631

/John S. Brusca/

Primary Examiner, Art Unit 1631

